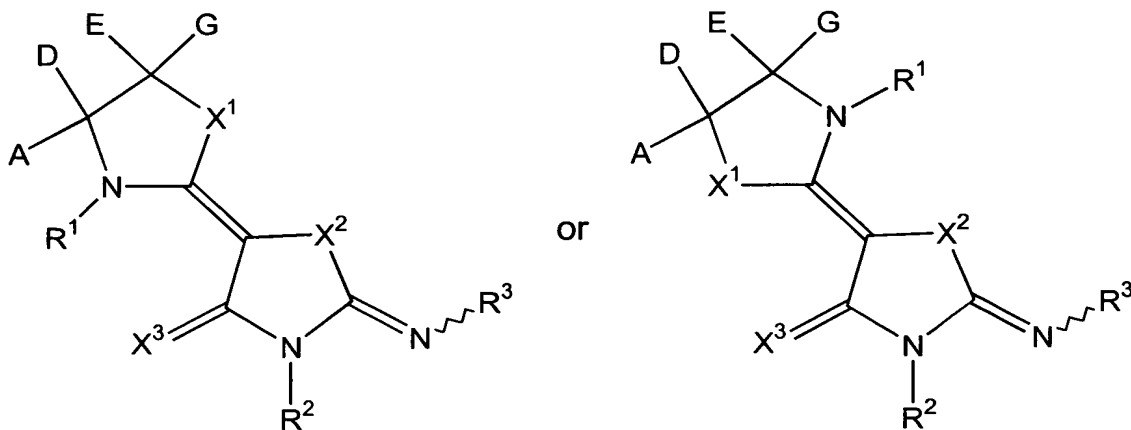


**WHAT IS CLAIMED IS:**

1. A pharmaceutical composition, comprising:
  - (a) a compound of formulae I:



- 5 or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

- (i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>, or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;
- D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted

- cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl,
- 5 substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or
- (ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene;
- 10 and the others of A, D, E and G are selected as in (i);
- $X^1$  and  $X^2$  are each independently selected from O, S,  $S(=O)$ ,  $S(=O)_2$ , Se,  $NR^5$ ,  $CR^6R^7$  and  $CR^8=CR^9$ ;
- $X^3$  is O, S, Se,  $NR^5$  or  $CR^6R^7$ ;
- $R^1$  and  $R^2$  are each independently selected from hydrogen, substituted
- 15 or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted
- 20 aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;
- $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or
- 25 unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted
- 30 heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;
- where
- $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or C(=J)R<sup>13</sup>;

J is O, S or NR<sup>14</sup>;

R<sup>13</sup> is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo, OR<sup>16</sup> and NR<sup>14</sup>R<sup>15</sup>;

R<sup>14</sup>, R<sup>15</sup> and R<sup>16</sup> are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl,

- heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, 5 aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocycloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, 10 alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'- 15 arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocabonyl, alkylaminothiocabonyl, 20 arylaminothiocabonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminomalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, 25 aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, 30 hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfonyloxy, alkylsulfonyloxy, arylsulfonyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,

- alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or
- 5 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the same atom, together form alkylene; and
- each Q<sup>1</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from Q<sup>2</sup>;
- 10 each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl,
- 15 aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl,
- 20 arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy,
- 25 dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-trialkylureido, amidino, alkylamidino, arylamidino, aminothiocabonyl,
- 30 alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,

- alkylarylaminooalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino,
- 5** alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano,
- 10** alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl,
- 15** alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;
- 20** each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;  
 $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form
- 25** alkylene, azaalkylene, oxaalkylene or thiaalkylene;  
 $R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;  
 $R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and
- 30**  $R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ ; and
- (b) one or more of the following: an antihyperlipidemic agent, a plasma HDL-raising agent, an anti-hypercholesterolemic agent, a cholesterol

biosynthesis inhibitor, an acyl-coenzyme A:cholesterol acyltransferase (ACAT) inhibitor, probucol, raloxifene, nicotinic acid, niacinamide, a cholesterol absorption inhibitor, a bile acid sequestrant, a low density lipoprotein receptor inducer, clofibrate, fenofibrate, benzofibrate, ciprofibrate, gemfibrozil, vitamin

**5** B<sub>6</sub>, vitamin B<sub>12</sub>, an anti-oxidant vitamin, a  $\beta$ -blocker, an anti-diabetes agent, an angiotensin II antagonist, an angiotensin converting enzyme inhibitor, a platelet aggregation inhibitor, a fibrinogen receptor antagonist, aspirin or a fibric acid derivative.

2. The composition of claim 1, wherein the cholesterol biosynthesis  
10 inhibitor is an HMG CoA reductase inhibitor.

3. The composition of claim 2, wherein the HMG CoA reductase inhibitor is lovastatin, simvastatin, pravastatin, fluvastatin, atorvastatin or rivastatin.

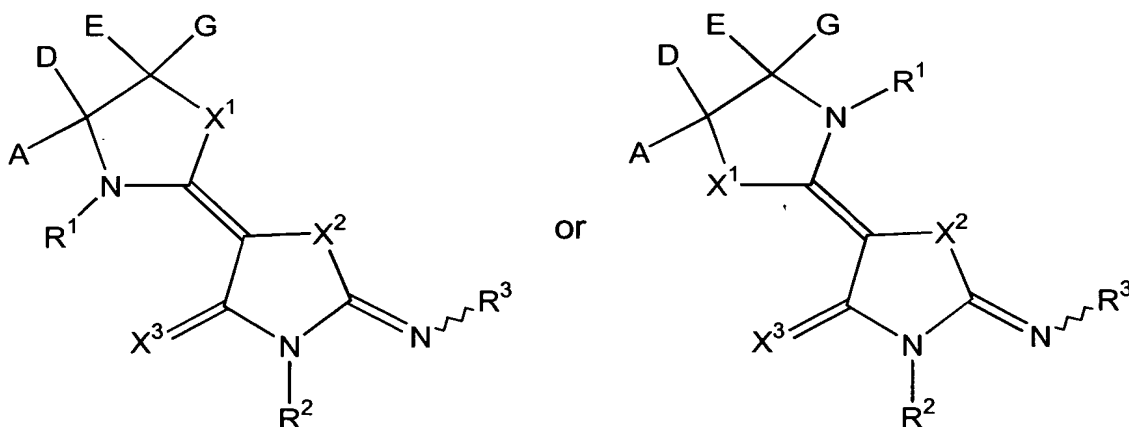
4. The composition of claim 3, wherein the HMG CoA reductase inhibitor is lovastatin or simvastatin.

5. The composition of claim 1, wherein the bile acid sequestrant is an anion exchange resin or a quaternary amine.

6. The composition of claim 1, wherein the quaternary amine is cholestyramine or colestipol.

**20**        7.        A pharmaceutical composition, comprising:

(a) a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

**25** (i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

- substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $\text{OR}^{10}$ ,  $\text{SR}^{10}$ ,  $\text{S(=O)R}^{13}$ ,  $\text{S(=O)}_2\text{R}^{13}$ ,  $\text{NR}^{11}\text{R}^{12}$  and  $\text{C(=J)R}^{13}$ , or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

- D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or
- (ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);
- $\text{X}^1$  and  $\text{X}^2$  are each independently selected from O, S,  $\text{S(=O)}$ ,  $\text{S(=O)}_2$ , Se,  $\text{NR}^5$ ,  $\text{CR}^6\text{R}^7$  and  $\text{CR}^8=\text{CR}^9$ ;
- $\text{X}^3$  is O, S, Se,  $\text{NR}^5$  or  $\text{CR}^6\text{R}^7$ ;
- $\text{R}^1$  and  $\text{R}^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or



unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

R<sup>3</sup> is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

where

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or C(=J)R<sup>13</sup>;

J is O, S or NR<sup>14</sup>;

- $R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;
- $R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;
- where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or more substituents each independently selected from  $Q^1$ , where  $Q^1$  is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkylidiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxy carbonyl, aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-

- arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino,
- 5** alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino,
- 10** arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,
- 15** hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyno, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylamino sulfonyloxy,
- 20** alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylamino sulfonyl or alkylarylaminosulfonyl; or two  $Q^1$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or
- 25** alkylenedithioxy where y is 1 or 2; or two  $Q^1$  groups, which substitute the same atom, together form alkylene; and
- each  $Q^1$  is independently unsubstituted or substituted with one or more substituents each independently selected from  $Q^2$ ;
- each  $Q^2$  is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,
- 30** nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl,

- aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl,
- 5** arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy,
- 10** aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-
- 15** diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocabonyl, alkylaminothiocabonyl, arylaminothiocabonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,
- 20** alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,
- 25** heterocyclylsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,
- 30** hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl,

alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q<sup>2</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>2</sup> groups, which  
 5 substitute the same atom, together form alkylene;

each Q<sup>2</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;

R<sup>50</sup> is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>, where R<sup>70</sup> and R<sup>71</sup> are each independently hydrogen, alkyl, aralkyl,  
 10 aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R<sup>70</sup> and R<sup>71</sup> together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R<sup>51</sup>, R<sup>52</sup> and R<sup>53</sup> are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R<sup>60</sup> is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl,  
 15 heterocyclyl or heterocyclylalkyl; and

R<sup>63</sup> is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>;  
 and

(b) one or more of the following: an antihyperlipidemic agent, a plasma HDL-raising agent, an antihypercholesterolemic agent, an HMG-CoA  
 20 synthase inhibitor, a squalene epoxidase inhibitor, a squalene synthetase inhibitor, an acyl-coenzyme A cholesterol acyltransferase inhibitor, probucol, nicotinic acid or a salt thereof, niacinamide, a cholesterol absorption inhibitor, a bile acid sequestrant anion exchange resin, a low density lipoprotein receptor inducer, a fibrate, vitamin B<sub>6</sub> or a pharmaceutically acceptable salt  
 25 thereof, vitamin B<sub>12</sub>, vitamin B<sub>3</sub>, an anti-oxidant vitamin, a beta-blocker, an angiotensin II antagonist, an angiotensin converting enzyme inhibitor, a platelet aggregation inhibitor, or aspirin.

8. The composition of claim 7, wherein the antihypercholesterolemic agent is a cholesterol biosynthesis inhibitor.

30 9. The composition of claim 8, wherein the cholesterol biosynthesis inhibitor is an hydroxymethylglutaryl CoA reductase inhibitor.

10. The composition of claim 9, wherein the hydroxymethylglutaryl CoA reductase inhibitor is lovastatin, simvastatin, pravastatin, fluvastatin, or atorvastatin.

11. The composition of claim 7, wherein the acyl-coenzyme A  
5 cholesterol acyltransferase inhibitor is melinamide.

12. The composition of claim 7, wherein the cholesterol absorption inhibitor is  $\beta$ -sitosterol.

13. The composition of claim 7, wherein the bile acid sequestrant anion exchange resin is cholestyramine, colestipol or a dialkylaminoalkyl  
10 derivative of a cross-linked dextran.

14. The composition of claim 7, wherein the fibrate is clofibrate, bezafibrate, fenofibrate, or gemfibrozil.

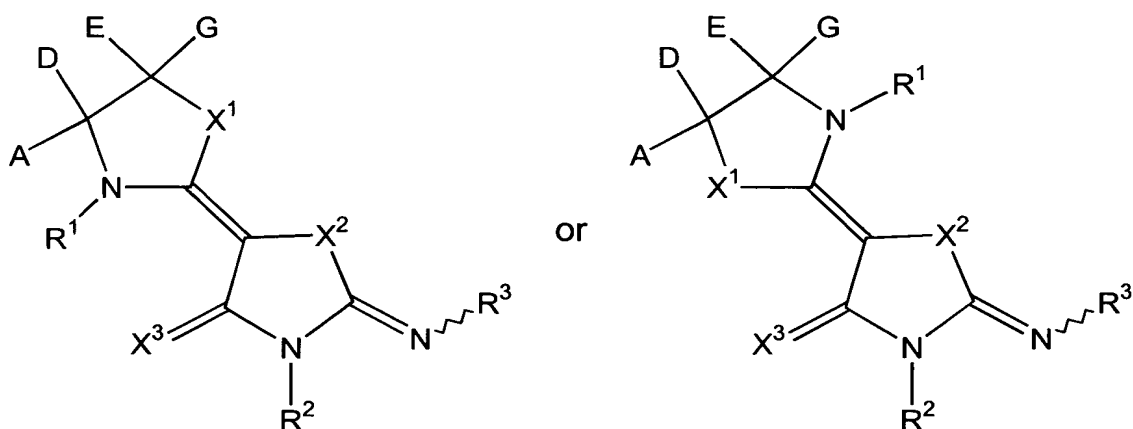
15. The composition of claim 7, wherein the anti-oxidant vitamin is vitamin C, vitamin E or beta carotene.

16. The composition of claim 7, wherein the platelet aggregation inhibitor is a fibrinogen receptor antagonist.

17. The composition of claim 16, wherein the fibrinogen receptor antagonist is a glycoprotein IIb/IIIa fibrinogen receptor antagonist.

18. A pharmaceutical composition, comprising:

20 (a) a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen,  
25 substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,  
substituted or unsubstituted alkynyl, substituted or unsubstituted

cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ , or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

(ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

$X^1$  and  $X^2$  are each independently selected from O, S,  $S(=O)$ ,  $S(=O)_2$ , Se,  $NR^5$ ,  $CR^6R^7$  and  $CR^8=CR^9$ ;

$X^3$  is O, S, Se,  $NR^5$  or  $CR^6R^7$ ;

$R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or

unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

R<sup>3</sup> is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

where

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or C(=J)R<sup>13</sup>;

J is O, S or NR<sup>14</sup>;

R<sup>13</sup> is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl,



substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo, OR<sup>16</sup> and NR<sup>14</sup>R<sup>15</sup>;

R<sup>14</sup>, R<sup>15</sup> and R<sup>16</sup> are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

- where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto,
- hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene,
- alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclioxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido,

- N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl,
- 5** arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino,
- 10** heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyno, isothiocyano, alkylsulfinyloxy,
- 15** alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylamino sulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl,
- 20** dialkylaminosulfonyl, arylaminosulfonyl, diarylamino sulfonyl or alkylarylaminosulfonyl; or two  $Q^1$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^1$  groups, which substitute the same atom, together form alkylene; and
- 25** each  $Q^1$  is independently unsubstituted or substituted with one or more substituents each independently selected from  $Q^2$ ;
- each  $Q^2$  is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2
- 30** double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl,

- heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy,
- 5** aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy,
- 10** guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-
- 15** triarylureido, amidino, alkylamidino, arylamidino, aminothiocabonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino,
- 20** aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl,
- 25** alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy,
- 30** diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^2$  groups, which

substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>2</sup> groups, which substitute the same atom, together form alkylene;

each Q<sup>2</sup> is independently unsubstituted or substituted with one or more  
 5 substituents each independently selected from alkyl, halo and pseudohalo;

R<sup>50</sup> is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>, where R<sup>70</sup> and R<sup>71</sup> are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R<sup>70</sup> and R<sup>71</sup> together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

10 R<sup>51</sup>, R<sup>52</sup> and R<sup>53</sup> are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclalkyl;

R<sup>60</sup> is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclalkyl; and

R<sup>63</sup> is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>;  
 15 and

(b) one or more of the following: a sulfonylurea, a biguanides, a thiazolidinedione, an insulin sensitizer, dehydroepiandrosterone or its conjugated sulfate ester, an antiglucoctocorticoid, a TNF $\alpha$  inhibitor, an  $\alpha$ -glucosidase inhibitor, pramlintide, an insulin secretagogue, or insulin.

20 19. The composition of claim 18, wherein the sulfonylurea is chlorpropamide, tolbutamide, acetohexamide, tolazamide, glyburide, glliclazide, glynase, glimepiride, or glipizide.

20. The composition of claim 18, wherein the biguanide is metformin.

25 21. The composition of claim 18, wherein the thiazolidinedione is ciglitazone, pioglitazone, troglitazone, or rosiglitazone.

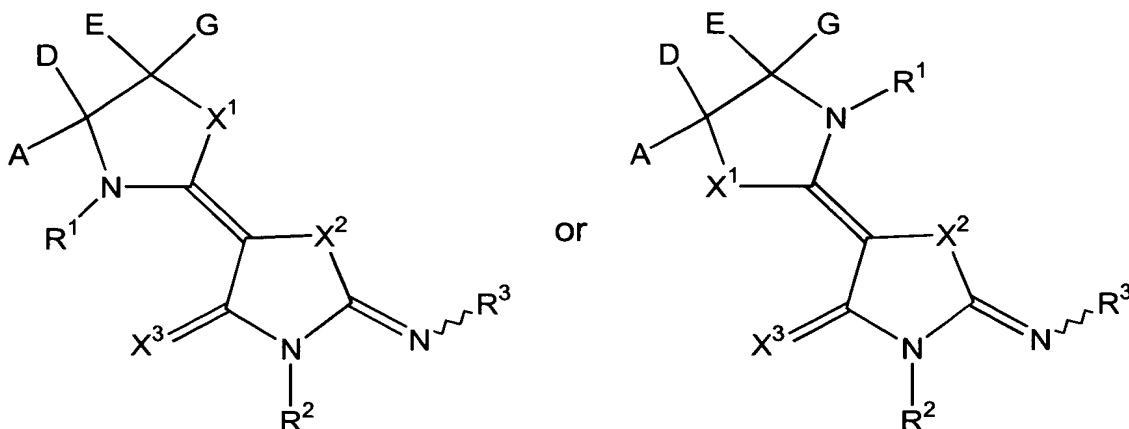
22. The composition of claim 18, wherein the insulin sensitizer is a selective or non-selective activator of PPAR $\alpha$ , PPAR $\beta$  or PPAR $\gamma$ .

23. The composition of claim 18, wherein the  $\alpha$ -glucosidase inhibitor  
 30 is acarbose, miglitol, or voglibose.

24. The composition of claim 18, wherein the insulin secretagogue is repaglinide, gliquidone, or nateglinide.

25. A pharmaceutical composition, comprising:

(a) a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

- 5 (i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>,  
 10 or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

- 20 D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted
- 25

- heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or
- 5 (ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);
- $X^1$  and  $X^2$  are each independently selected from O, S,  $S(=O)$ ,  $S(=O)_2$ ,  
 10 Se,  $NR^5$ ,  $CR^6R^7$  and  $CR^8=CR^9$ ;  
 $X^3$  is O, S, Se,  $NR^5$  or  $CR^6R^7$ ;  
 $R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or  
 15 unsubstituted heterocyclalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  
 20  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;  
 $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl,  
 25 substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;  
 where
- 30  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted

cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo,  $\text{OR}^{10}$ ,  $\text{NR}^{14}\text{R}^{15}$  and  $\text{C}(=\text{J})\text{R}^{13}$ ;

- 5**  $\text{R}^{10}$ ,  $\text{R}^{11}$  and  $\text{R}^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted
- 10** aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $\text{C}(=\text{J})\text{R}^{13}$ ;
- $\text{J}$  is O, S or  $\text{NR}^{14}$ ;
- $\text{R}^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl,
- 15** substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $\text{OR}^{16}$  and  $\text{NR}^{14}\text{R}^{15}$ ;
- 20**  $\text{R}^{14}$ ,  $\text{R}^{15}$  and  $\text{R}^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;
- where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocycl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl,
- 25** heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G,  $\text{R}^1$ ,  $\text{R}^2$ ,  $\text{R}^3$ ,  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ ,  $\text{R}^8$ ,  $\text{R}^9$ ,  $\text{R}^{10}$ ,  $\text{R}^{11}$ ,  $\text{R}^{12}$  and  $\text{R}^{13}$  are unsubstituted or substituted with one or more substituents each independently selected from  $\text{Q}^1$ , where  $\text{Q}^1$  is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl,
- 30** aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocycl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene,

- alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl,
- 5** arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy,
- 10** alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido,
- 15** N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocabonyl, alkylaminothiocabonyl, arylaminothiocabonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino,
- 20** haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido,
- 25**  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy,
- 30** alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylamino sulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl,



- dialkylaminosulfonyl, arylaminosulfonyl, diarylamino sulfonyl or alkylarylamino sulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the
- 5** same atom, together form alkylene; and
- each Q<sup>1</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from Q<sup>2</sup>;
- each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl,
- 10** haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl,
- 15** heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylamino carbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy,
- 20** perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylamino carbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido,
- 25** N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-trialkylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl,
- 30** alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino,

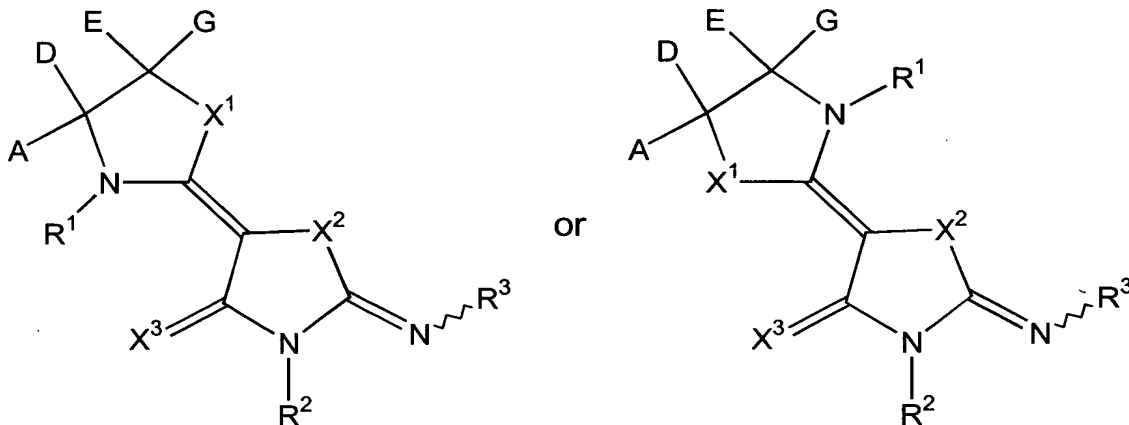
- aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  
**5**  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy,  
**10** alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^2$  groups, which  
**15** substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;  
each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;  
**20**  $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;  
 $R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl,  
**25** heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;  
 $R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and  
 $R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ ;  
and  
**30** (b) one or more of the following: phenylpropanolamine, phentermine, diethylpropion, mazindol, fenfluramine, dexfenfluramine, phentiramine, a  $\beta_3$  adrenoceptor agonist, sibutramine, a gastrointestinal lipase inhibitor, a leptin, neuropeptide Y, enterostatin, cholecystokinin, bombesin,

amylin, a histamine H<sub>3</sub> receptor, a dopamine D<sub>2</sub> receptor, melanocyte stimulating hormone, corticotrophin releasing factor, galanin or gamma amino butyric acid.

26. The composition of claim 25, wherein the gastrointestinal lipase inhibitor is orlistat.

27. A pharmaceutical composition, comprising:

(a) a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

- 10 A, D, E and G are selected from (i) or (ii) as follows:
- (i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>,
- 15 or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene,
- 20 substituted or unsubstituted 1,3-butadienylene, substituted or
- 25

unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

- D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or
- (ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene;
- and the others of A, D, E and G are selected as in (i);
- $X^1$  and  $X^2$  are each independently selected from O, S,  $S(=O)$ ,  $S(=O)_2$ , Se,  $NR^5$ ,  $CR^6R^7$  and  $CR^8=CR^9$ ;
- $X^3$  is O, S, Se,  $NR^5$  or  $CR^6R^7$ ;
- $R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;
- $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted

aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ; where

- $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

- $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

J is O, S or  $NR^{14}$ ;

- $R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

- where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or

- more substituents each independently selected from  $Q^1$ , where  $Q^1$  is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl
- 5** containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy,
- 15** alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl,
- 25** arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino,
- 30** heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,

- hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy,
- 5** dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylamino sulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylamino sulfonyl or alkylarylaminosulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or
- 10** 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the same atom, together form alkylene; and
- each Q<sup>1</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from Q<sup>2</sup>;
- 15** each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl,
- 20** aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl,
- 25** arylaminocarbonyl, diarylamino carbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy,
- 30** dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylamino carbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-

- diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl,
- 5** alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxy arylcarbonylamino, aryloxy carbonylamino,
- 10** alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyno, isothiocyano,
- 15** alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylamino sulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl,
- 20** alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylamino sulfonyl or alkylarylaminosulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;
- 25** each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;
- $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form
- 30** alkylene, azaalkylene, oxaalkylene or thiaalkylene;
- $R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;



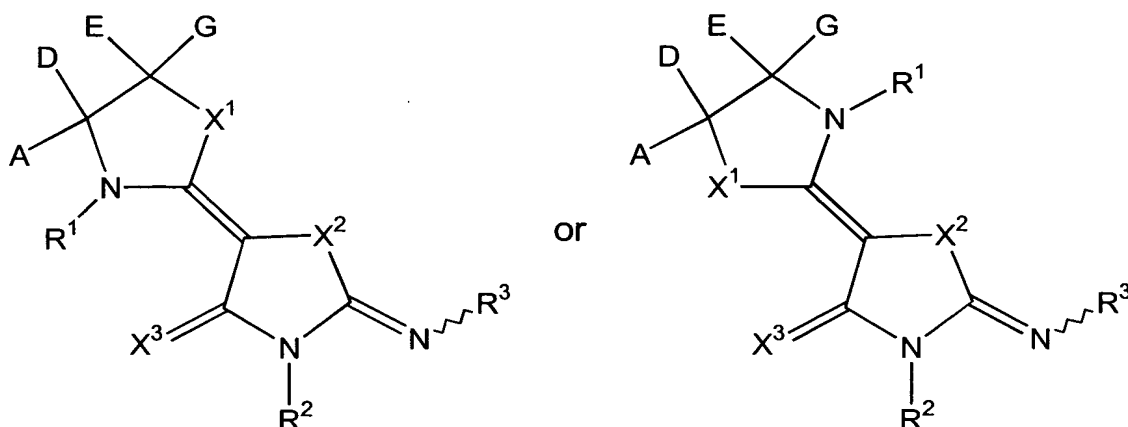
R<sup>60</sup> is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

R<sup>63</sup> is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>;  
and

- 5 (b) one or more of the following: ursodeoxycholic acid, a corticosteroid, an anti-infective agent, an anti-viral agent, vitamin D, vitamin A, phenobarbital, cholestyramine, UV light, an antihistamine, an oral opiate receptor antagonist or a biphosphate.

28. The composition of claim 27, wherein the anti-infective agent is  
10 rifampin, rifadin, or rimactane.

29. A method for decreasing hyperglycemia and/or insulin resistance, comprising administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

- 15 A, D, E and G are selected from (i) or (ii) as follows:
- (i) A and G are each independently selected from hydrogen,  
substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,  
substituted or unsubstituted alkynyl, substituted or unsubstituted  
cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or  
20 unsubstituted cycloalkylalkyl, substituted or unsubstituted  
heterocyclylalkyl, substituted or unsubstituted aryl, substituted or  
unsubstituted heteroaryl, substituted or unsubstituted aralkyl,  
substituted or unsubstituted heteroaralkyl, substituted or unsubstituted  
heteroarylum, substituted or unsubstituted heteroarylumalkyl, halo,  
25 pseudohalo,  $\text{OR}^{10}$ ,  $\text{SR}^{10}$ ,  $\text{S(=O)R}^{13}$ ,  $\text{S(=O)}_2\text{R}^{13}$ ,  $\text{NR}^{11}\text{R}^{12}$  and  $\text{C(=J)R}^{13}$ ,  
or A and G together form substituted or unsubstituted alkylene.

substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

(ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

$X^1$  and  $X^2$  are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;

$X^3$  is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

R<sup>1</sup> and R<sup>2</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

R<sup>3</sup> is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or

unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>; where

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or C(=J)R<sup>13</sup>;

J is O, S or NR<sup>14</sup>;

R<sup>13</sup> is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo, OR<sup>16</sup> and NR<sup>14</sup>R<sup>15</sup>;

R<sup>14</sup>, R<sup>15</sup> and R<sup>16</sup> are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

- where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylum, aralkyl, heteroaralkyl and heteroarylumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or
- 5 more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl,
- 10 heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl,
- 15 dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy,
- 20 aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl,
- 30 arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino,

- aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,
- 5** hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,
- 10** alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^1$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or
- 15** alkylenedithioxy where y is 1 or 2; or two  $Q^1$  groups, which substitute the same atom, together form alkylene; and
- each  $Q^1$  is independently unsubstituted or substituted with one or more substituents each independently selected from  $Q^2$ ;
- each  $Q^2$  is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,
- 20** nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkylidiarylsilyl,
- 25** triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy,
- 30** aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy,

- dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,
- 10** alkylarylaminooalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,
- 15** heterocyclylsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,
- 20** hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl,
- 25** diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;
- each  $Q^2$  is independently unsubstituted or substituted with one or more
- 30** substituents each independently selected from alkyl, halo and pseudohalo;
- $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl,

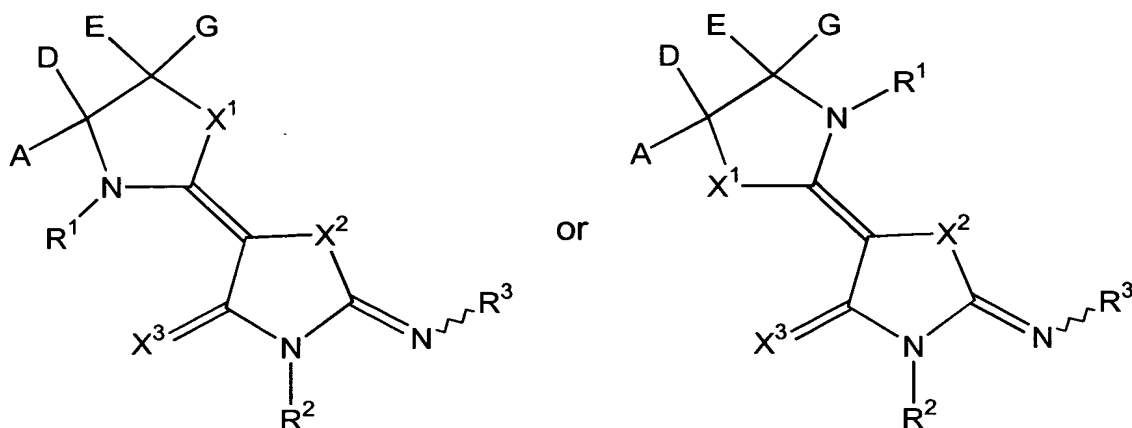
aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

$R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclalkyl;

5  $R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclalkyl; and

$R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ .

30. A method for treatment, prevention or amelioration of one or more symptoms or complications of type II diabetes, comprising administering  
10 a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen,  
15 substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or  
20 unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ , or A and G together form substituted or unsubstituted alkylene,  
25 substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or

unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

- 5           D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted
- 10       heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or
- (ii)    A and D; or E and G; together form substituted or unsubstituted
- 15       alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);
- $X^1$  and  $X^2$  are each independently selected from O, S,  $S(=O)$ ,  $S(=O)_2$ , Se,  $NR^5$ ,  $CR^6R^7$  and  $CR^8=CR^9$ ;
- 20        $X^3$  is O, S, Se,  $NR^5$  or  $CR^6R^7$ ;
- $R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,
- 25       substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;
- 30        $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl,



substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;

5 where

$R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

10  $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

15 J is O, S or  $NR^{14}$ ;

$R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

25  $R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl,

- heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto,
- 5** hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene,
- 10** alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy,
- 15** heterocycloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido,
- 20** ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino,
- 25** arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino,
- 30** alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido,

- N<sup>+</sup>R<sup>51</sup>R<sup>52</sup>R<sup>53</sup>, P(R<sup>50</sup>)<sub>2</sub>, P(=O)(R<sup>50</sup>)<sub>2</sub>, OP(=O)(R<sup>50</sup>)<sub>2</sub>, -NR<sup>60</sup>C(=O)R<sup>63</sup>,  
dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,  
hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio,  
hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy,  
5 alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy,  
alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy,  
dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,  
alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl,  
hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl,  
10 dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or  
alkylarylaminosulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or  
1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or  
alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the  
same atom, together form alkylene; and  
15 each Q<sup>1</sup> is independently unsubstituted or substituted with one or more  
substituents each independently selected from Q<sup>2</sup>;  
each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,  
nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl,  
haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2  
20 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl,  
cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl,  
aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkylarylsilyl,  
trialkylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl,  
heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy, carbonyl,  
25 aryloxy, heteroaryloxy, heteroaralkoxy, heterocycloxy, cycloalkoxy,  
perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy,  
arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy, carbonyloxy,  
aralkoxy, heteroaryloxy, heteroaralkoxy, heterocycloxy, cycloalkoxy,  
30 arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy, carbonyloxy,  
aralkoxy, heteroaryloxy, heteroaralkoxy, heterocycloxy, cycloalkoxy,  
dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy,  
guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido,

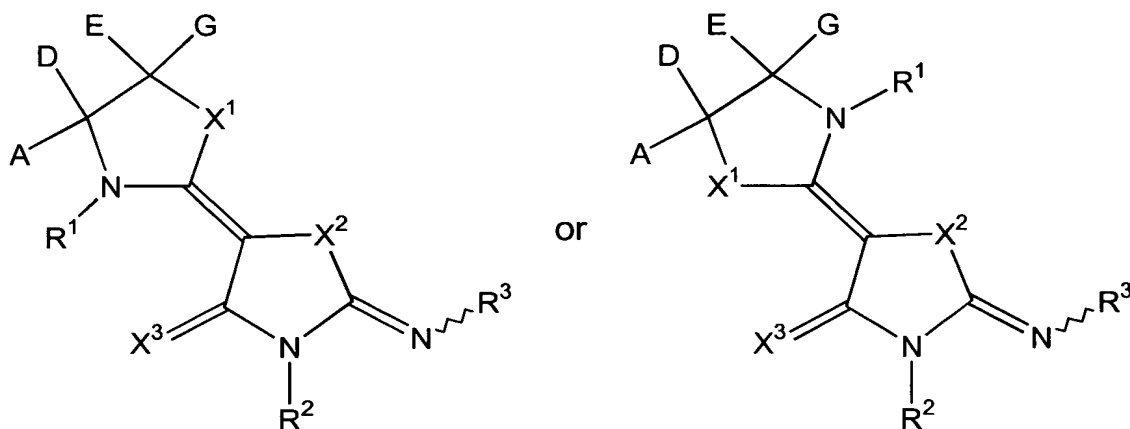
- N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylulfonylamino, heterocyclulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyno, isothiocyno, alkylsulfonyloxy, alkylsulfonyloxy, arylsulfonyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfonyl, alkylsulfonyl, arylsulfonyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;
- each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;
- $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

$R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclalkyl;

$R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclalkyl; and

5  $R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ .

31. A method of modulating atherosclerosis, comprising administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

10 A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ,

15 or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or

25

unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

(ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

$X^1$  and  $X^2$  are each independently selected from O, S,  $S(=O)$ ,  $S(=O)_2$ , Se,  $NR^5$ ,  $CR^6R^7$  and  $CR^8=CR^9$ ;

$X^3$  is O, S, Se,  $NR^5$  or  $CR^6R^7$ ;

$R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;

$R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted

aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ; where

- $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

- $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

J is O, S or  $NR^{14}$ ;

- $R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

- where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or

- more substituents each independently selected from  $Q^1$ , where  $Q^1$  is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl
- 5 containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl,
- 10 aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy,
- 15 alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-
- 20 arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl,
- 25 arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino,
- 30 aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,



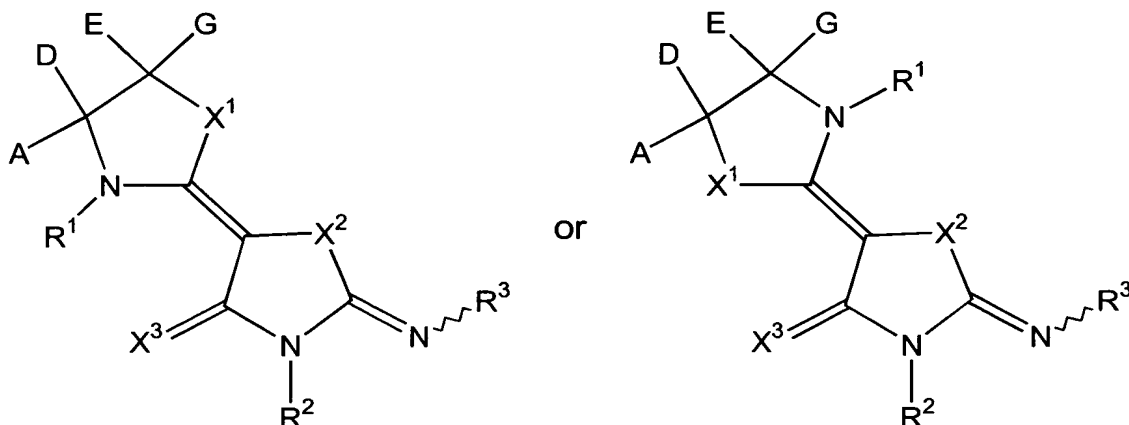
- hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy,
- 5** dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylamino sulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylamino sulfonyl or alkylarylaminosulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or
- 10** 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the same atom, together form alkylene; and
- each Q<sup>1</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from Q<sup>2</sup>;
- 15** each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl,
- 20** aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl,
- 25** arylaminocarbonyl, diarylamino carbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy,
- 30** dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylamino carbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-

- diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl,
- 5** alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino,
- 10** alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano,
- 15** alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminoalkyl, alkylarylaminoalkyl, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl,
- 20** alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminoalkyl or alkylarylaminoalkyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;
- 25** each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;
- $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form
- 30** alkylene, azaalkylene, oxaalkylene or thiaalkylene;
- $R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

$R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

$R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ .

32. A method of treating, preventing, or ameliorating obesity or complications thereof, comprising administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

- (i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ , or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

- D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or
- (ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);
- $X^1$  and  $X^2$  are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;
- $X^3$  is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;
- $R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;
- $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted

heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ; where

- $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

- $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

J is O, S or  $NR^{14}$ ;

- $R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

- where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or more substituents each independently selected from  $Q^1$ , where  $Q^1$  is halo,

- pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl,
- 5** heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl,
- 10** dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy,
- 15** aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl,
- 25** arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino,
- 30** heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio,

- hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylamino sulfonyloxy,
- 5** alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylamino sulfonyl or alkylarylaminosulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or
- 10** alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the same atom, together form alkylene; and
- each Q<sup>1</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from Q<sup>2</sup>;
- each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,
- 15** nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl,
- 20** triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxy carbonyl, aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylamino carbonyl, arylalkylaminocarbonyl, alkoxy,
- 25** aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylamino carbonyloxy,
- 30** guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-

- diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,
- 5** alkylarylaminomethyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroaryl sulfonylamino,
- 10** heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,
- 15** hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylamino sulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl,
- 20** diarylamino sulfonyl or alkylarylaminosulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;
- each  $Q^2$  is independently unsubstituted or substituted with one or more
- 25** substituents each independently selected from alkyl, halo and pseudohalo;
- $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;
- 30**  $R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;
- $R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and



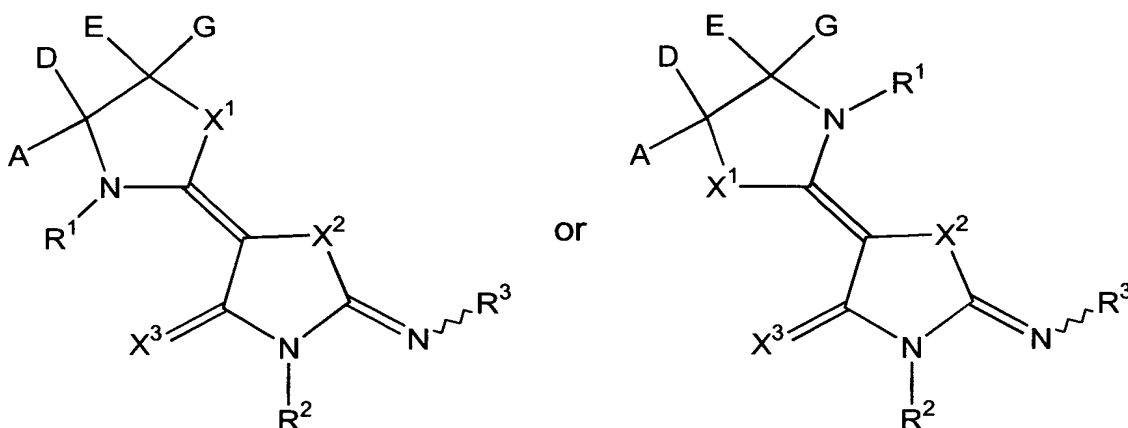
$R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ .

33. A method of treating, preventing, or ameliorating one or more symptoms of a disease or disorder that is modulated or otherwise affected by nuclear receptor activity or in which nuclear receptor activity is implicated,

5 comprising administering a pharmaceutical composition of claim 1.

34. A method of treating, preventing, or ameliorating one or more symptoms of a disease or disorder that is modulated or otherwise affected by nuclear receptor activity or in which nuclear receptor activity is implicated, comprising:

10 (a) administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

$A$ ,  $D$ ,  $E$  and  $G$  are selected from (i) or (ii) as follows:

(i)  $A$  and  $G$  are each independently selected from hydrogen,  
 15 substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,  
 substituted or unsubstituted alkynyl, substituted or unsubstituted  
 cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or  
 unsubstituted cycloalkylalkyl, substituted or unsubstituted  
 heterocyclalkyl, substituted or unsubstituted aryl, substituted or  
 20 unsubstituted heteroaryl, substituted or unsubstituted aralkyl,  
 substituted or unsubstituted heteroaralkyl, substituted or unsubstituted  
 heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo,  
 pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ,  
 or  $A$  and  $G$  together form substituted or unsubstituted alkylene,  
 25 substituted or unsubstituted azaalkylene, substituted or unsubstituted  
 oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or

unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

- 5** D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted
- 10** heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or
- (ii) A and D; or E and G; together form substituted or unsubstituted
- 15** alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);
- $X^1$  and  $X^2$  are each independently selected from O, S,  $S(=O)$ ,  $S(=O)_2$ , Se,  $NR^5$ ,  $CR^6R^7$  and  $CR^8=CR^9$ ;
- 20**  $X^3$  is O, S, Se,  $NR^5$  or  $CR^6R^7$ ;
- $R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,
- 25** substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;
- 30**  $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl,

substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

5 where

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

10 R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or C(=J)R<sup>13</sup>;

J is O, S or NR<sup>14</sup>;

15 R<sup>13</sup> is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo, OR<sup>16</sup> and NR<sup>14</sup>R<sup>15</sup>;

20 R<sup>14</sup>, R<sup>15</sup> and R<sup>16</sup> are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl,

- heteroaralkyl and heteroarylalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto,
- 5** hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene,
- 10** alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy,
- 15** heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido,
- 20** ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino,
- 25** arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino,
- 30** alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido,

- N<sup>+</sup>R<sup>51</sup>R<sup>52</sup>R<sup>53</sup>, P(R<sup>50</sup>)<sub>2</sub>, P(=O)(R<sup>50</sup>)<sub>2</sub>, OP(=O)(R<sup>50</sup>)<sub>2</sub>, -NR<sup>60</sup>C(=O)R<sup>63</sup>, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy,
- 5** alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl,
- 10** dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the same atom, together form alkylene; and
- 15** each Q<sup>1</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from Q<sup>2</sup>;
- each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2
- 20** double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkylarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy, carbonyl,
- 25** aryloxy, heteroaryloxy, heteroaralkoxy, heterocycloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy, carbonyloxy,
- 30** aralkoxy, carbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, arylaminocarbonyloxy, diarylaminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido,

- N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;
- each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;
- $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

$R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclalkyl;

$R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclalkyl; and

- 5  $R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ ; and

- (b) simultaneously, subsequently, or previously administering one or more of the following: an antihyperlipidemic agent, a plasma HDL-raising agent, an anti-hypercholesterolemic agent, a cholesterol biosynthesis
- 10 inhibitor, an acyl-coenzyme A:cholesterol acyltransferase (ACAT) inhibitor, probucol, raloxifene, nicotinic acid, niacinamide, a cholesterol absorption inhibitor, a bile acid sequestrant, a low density lipoprotein receptor inducer, clofibrate, fenofibrate, benzofibrate, ciprofibrate, gemfibrozil, vitamin B<sub>6</sub>, vitamin B<sub>12</sub>, an anti-oxidant vitamin, a  $\beta$ -blocker, an anti-diabetes agent, an
- 15 angiotensin II antagonist, an angiotensin converting enzyme inhibitor, a platelet aggregation inhibitor, a fibrinogen receptor antagonist, aspirin or a fibric acid derivative.

35. The method of claim 33, wherein the disease or disorder is selected from hypercholesterolemia, hyperlipoproteinemia,
- 20 hypertriglyceridemia, lipodystrophy, hyperglycemia, diabetes mellitus, dyslipidemia, atherosclerosis, gallstone disease, acne vulgaris, acneiform skin conditions, diabetes, Parkinson's disease, cancer, Alzheimer's disease, inflammation, immunological disorders, lipid disorders, obesity, conditions characterized by a perturbed epidermal barrier function, hyperlipidemia,
- 25 cholestasis, peripheral occlusive disease, ischemic stroke, conditions of disturbed differentiation or excess proliferation of the epidermis or mucous membrane, and cardiovascular disorders.

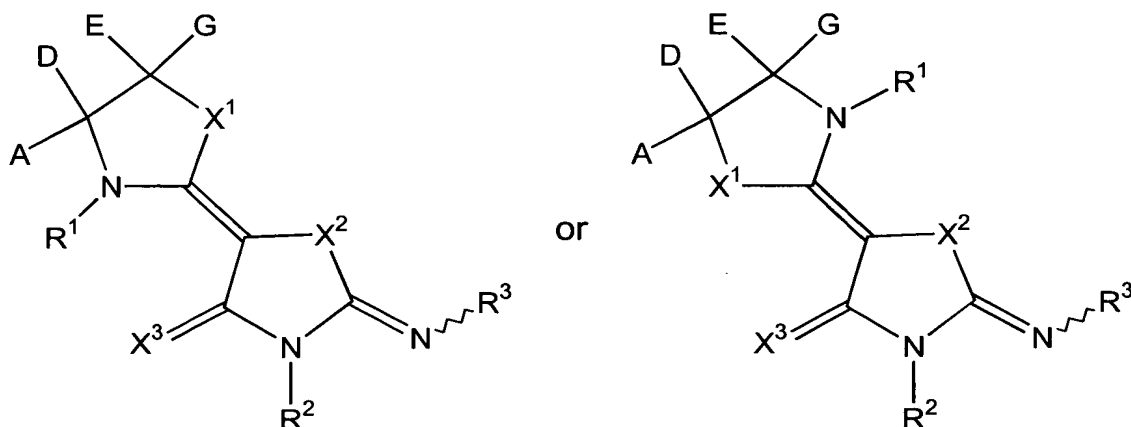
36. The method of claim 34, wherein the disease or disorder is selected from hypercholesterolemia, hyperlipoproteinemia,
- 30 hypertriglyceridemia, lipodystrophy, hyperglycemia, diabetes mellitus, dyslipidemia, atherosclerosis, gallstone disease, acne vulgaris, acneiform skin conditions, diabetes, Parkinson's disease, cancer, Alzheimer's disease, inflammation, immunological disorders, lipid disorders, obesity, conditions

characterized by a perturbed epidermal barrier function, hyperlipidemia, cholestasis, peripheral occlusive disease, ischemic stroke, conditions of disturbed differentiation or excess proliferation of the epidermis or mucous membrane, and cardiovascular disorders.

- 5            37. A method of treating, preventing, or ameliorating one or more symptoms of a disease or disorder which is affected by cholesterol, triglyceride, or bile acid levels, comprising administering a pharmaceutical composition of claim 1.

- 10           38. A method of treating, preventing, or ameliorating one or more symptoms of a disease or disorder which is affected by cholesterol, triglyceride, or bile acid levels, comprising:

(a) administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

- 15           A, D, E and G are selected from (i) or (ii) as follows:
- (i)        A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>,  
 20           or A and G together form substituted or unsubstituted alkylene,
- 25



substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or

(ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

$X^1$  and  $X^2$  are each independently selected from O, S,  $S(=O)$ ,  $S(=O)_2$ , Se,  $NR^5$ ,  $CR^6R^7$  and  $CR^8=CR^9$ ;

$X^3$  is O, S, Se,  $NR^5$  or  $CR^6R^7$ ;

$R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;

$R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or

unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>; where

R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup> and R<sup>9</sup> are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

R<sup>10</sup>, R<sup>11</sup> and R<sup>12</sup> are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or C(=J)R<sup>13</sup>;

J is O, S or NR<sup>14</sup>;

R<sup>13</sup> is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo, OR<sup>16</sup> and NR<sup>14</sup>R<sup>15</sup>;

R<sup>14</sup>, R<sup>15</sup> and R<sup>16</sup> are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

- where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or
- 5 more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl,
  - 10 heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl,
  - 15 dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocycloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy,
  - 20 aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl,
  - 30 arylaminoalkyl, diarylaminoalkyl, alkylaryl aminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylaryl amino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino,

- aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,
- 5** hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,
- 10** alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^1$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or
- 15** alkylenedithioxy where y is 1 or 2; or two  $Q^1$  groups, which substitute the same atom, together form alkylene; and
- each  $Q^1$  is independently unsubstituted or substituted with one or more substituents each independently selected from  $Q^2$ ;
- each  $Q^2$  is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,
- 20** nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkylidiarylsilyl,
- 25** triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy,
- 30** aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy,

- dialkylaminocarbonyloxy, alkylarylamino carbonyloxy, diarylamino carbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,
- 10** alkylarylaminoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,
- 15** heterocyclylsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,
- 20** hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylamino sulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl,
- 25** diarylamino sulfonyl or alkylarylamino sulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;
- each  $Q^2$  is independently unsubstituted or substituted with one or more
- 30** substituents each independently selected from alkyl, halo and pseudohalo;
- $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl,

aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

$R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclalkyl;

- 5  $R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclalkyl; and

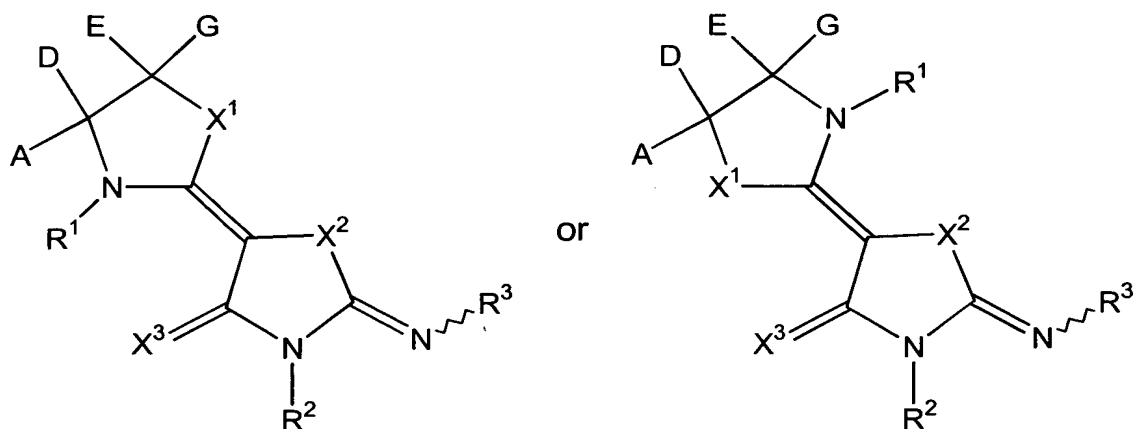
$R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ ; and

- (b) simultaneously, subsequently, or previously administering one  
 10 or more of the following: an antihyperlipidemic agent, a plasma HDL-raising agent, an anti-hypercholesterolemic agent, a cholesterol biosynthesis inhibitor, an acyl-coenzyme A:cholesterol acyltransferase (ACAT) inhibitor, probucol, raloxifene, nicotinic acid, niacinamide, a cholesterol absorption inhibitor, a bile acid sequestrant, a low density lipoprotein receptor inducer,  
 15 clofibrate, fenofibrate, benzofibrate, ciprofibrate, gemfibrizol, vitamin B<sub>6</sub>, vitamin B<sub>12</sub>, an anti-oxidant vitamin, a  $\beta$ -blocker, an anti-diabetes agent, an angiotensin II antagonist, an angiotensin converting enzyme inhibitor, a platelet aggregation inhibitor, a fibrinogen receptor antagonist, aspirin or a fibric acid derivative.

- 20 39. A method for decreasing hyperglycemia and/or insulin resistance, comprising administering the pharmaceutical composition of claim 18.

40 A method for decreasing hyperglycemia and/or insulin resistance, comprising:

- 25 (a) administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

- (i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>, or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;
- D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or
- (ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);

$X^1$  and  $X^2$  are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;

$X^3$  is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

$R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

$R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>; where

$R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

$R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,



substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

J is O, S or  $NR^{14}$ ;

- 5  $R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

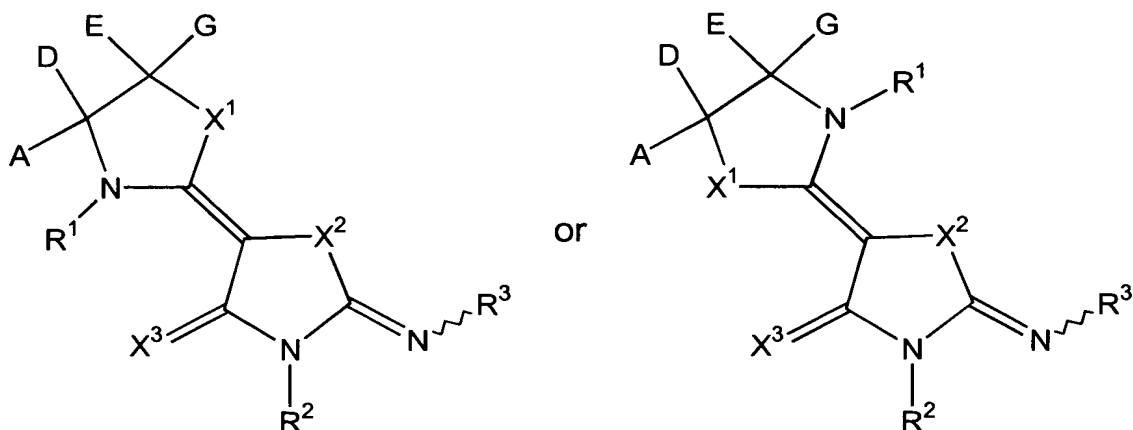
$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

- 15 where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocycl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or more substituents each independently selected from  $Q^1$ , where  $Q^1$  is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto,
- 20 hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocycl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl,
- 25 trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl,
- 30 arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy,

- aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxyulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxyulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^1$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^1$  groups, which substitute the same atom, together form alkylene; and
- each  $Q^1$  is independently unsubstituted or substituted with one or more substituents each independently selected from  $Q^2$ ;

- each  $Q^2$  is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl,
- 5** cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl,
- 10** arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy,
- 15** dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-
- 20** diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocabonyl, alkylaminothiocabonyl, arylaminothiocabonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,
- 25** alkylarylaminalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxy arylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,
- 30** heterocyclylsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano,

- alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q<sup>2</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>2</sup> groups, which substitute the same atom, together form alkylene;
- each Q<sup>2</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;
- R<sup>50</sup> is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>, where R<sup>70</sup> and R<sup>71</sup> are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R<sup>70</sup> and R<sup>71</sup> together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;
- R<sup>51</sup>, R<sup>52</sup> and R<sup>53</sup> are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;
- R<sup>60</sup> is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and
- R<sup>63</sup> is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>; and
- (b) subsequently, simultaneously, or previously administering one or more of the following: a sulfonylurea, a biguanides, a thiazolidinedione, an insulin sensitizer, dehydroepiandrosterone or its conjugated sulfate ester, an antigluco-corticoid, a TNF $\alpha$  inhibitor, an  $\alpha$ -glucosidase inhibitor, pramlintide, an insulin secretagogue, or insulin.
41. A method for treatment, prevention or amelioration of one or more symptoms or complications of type II diabetes, comprising administering a pharmaceutical composition of claim 18.
42. A method for treatment, prevention or amelioration of one or more symptoms or complications of type II diabetes, comprising:
- (a) administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

- (i) A and G are each independently selected from hydrogen,  
 5 substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,  
 substituted or unsubstituted alkynyl, substituted or unsubstituted  
 cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or  
 unsubstituted cycloalkylalkyl, substituted or unsubstituted  
 heterocyclylalkyl, substituted or unsubstituted aryl, substituted or  
 10 unsubstituted heteroaryl, substituted or unsubstituted aralkyl,  
 substituted or unsubstituted heteroaralkyl, substituted or unsubstituted  
 heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo,  
 pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>,  
 or A and G together form substituted or unsubstituted alkylene,  
 15 substituted or unsubstituted azaalkylene, substituted or unsubstituted  
 oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or  
 unsubstituted alkenylene, substituted or unsubstituted alkynylene,  
 substituted or unsubstituted 1,3-butadienylene, substituted or  
 unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted  
 20 2-aza-1,3-butadienylene;

- D and E are each independently selected from hydrogen,  
 substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,  
 substituted or unsubstituted alkynyl, substituted or unsubstituted  
 cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or  
 25 unsubstituted cycloalkylalkyl, substituted or unsubstituted  
 heterocyclylalkyl, substituted or unsubstituted aryl, substituted or

- unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or
- (ii) A and D; or E and G; together form substituted or unsubstituted
- 5** alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);
- $X^1$  and  $X^2$  are each independently selected from O, S,  $S(=O)$ ,  $S(=O)_2$ , Se,  $NR^5$ ,  $CR^6R^7$  and  $CR^8=CR^9$ ;
- 10**  $X^3$  is O, S, Se,  $NR^5$  or  $CR^6R^7$ ;
- $R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,
- 15** substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;
- 20**  $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl,
- 25** substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;
- where
- $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen,
- 30** substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or

unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

- $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

J is O, S or  $NR^{14}$ ;

- $R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

- $R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

- where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or more substituents each independently selected from  $Q^1$ , where  $Q^1$  is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl,

- alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy,
- 5** heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido,
- 10** ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino,
- 15** arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino,
- 20** alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ ,
- 25** dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy,
- 30** dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or



alkylarylaminosulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the same atom, together form alkylene; and

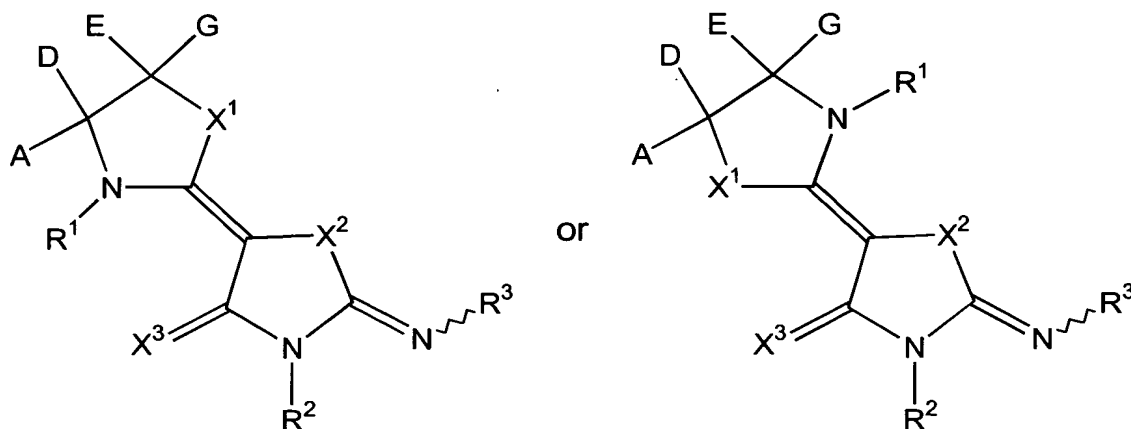
- 5           each Q<sup>1</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from Q<sup>2</sup>;  
               each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2  
 10 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl,  
 15 aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy,  
 20 arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido,  
 25 N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocabonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl,  
 30 alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminooalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl,

- aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl,
- 5** alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy,
- 10** diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy,
- 15** thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;
- each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;
- $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or
- 20**  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;
- $R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;
- 25**  $R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and
- $R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ ; and
- (b) subsequently, simultaneously, or previously administering one
- 30** or more of the following: a sulfonylurea, a biguanides, a thiazolidinedione, an insulin sensitizer, dehydroepiandrosterone or its conjugated sulfate ester, an antigluccorticoid, a  $TNF\alpha$  inhibitor, an  $\alpha$ -glucosidase inhibitor, pramlintide, an insulin secretagogue, or insulin.

43. A method of modulating atherosclerosis, comprising administering a pharmaceutical composition of claim 7.

44. A method of modulating atherosclerosis, comprising:

(a) administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

(i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>, or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;

D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,

- substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or
- (ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);
- $X^1$  and  $X^2$  are each independently selected from O, S,  $S(=O)$ ,  $S(=O)_2$ , Se,  $NR^5$ ,  $CR^6R^7$  and  $CR^8=CR^9$ ;
- $X^3$  is O, S, Se,  $NR^5$  or  $CR^6R^7$ ;
- $R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;
- $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;
- where

$R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

$R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

J is O, S or  $NR^{14}$ ;

$R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or more substituents each independently selected from  $Q^1$ , where  $Q^1$  is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl,

- aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene,
- 5 alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy,
- 10 heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido,
- 15 ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino,
- 20 arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino,
- 25 alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ ,
- 30 dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy,

- alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylamino sulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl,
- 5** dialkylaminosulfonyl, arylaminosulfonyl, diarylamino sulfonyl or alkylarylaminosulfonyl; or two Q<sup>1</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two Q<sup>1</sup> groups, which substitute the same atom, together form alkylene; and
- 10** each Q<sup>1</sup> is independently unsubstituted or substituted with one or more substituents each independently selected from Q<sup>2</sup>;
- each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2
- 15** double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl,
- 20** aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylamino carbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy,
- 25** arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylamino carbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido,
- 30** N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl,

- alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxycarbonylamino,
- 5** aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl,
- 10** alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy,
- 15** diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy,
- 20** thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;
- each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;
- $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or
- 25**  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;
- $R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;
- 30**  $R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and
- $R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ ; and

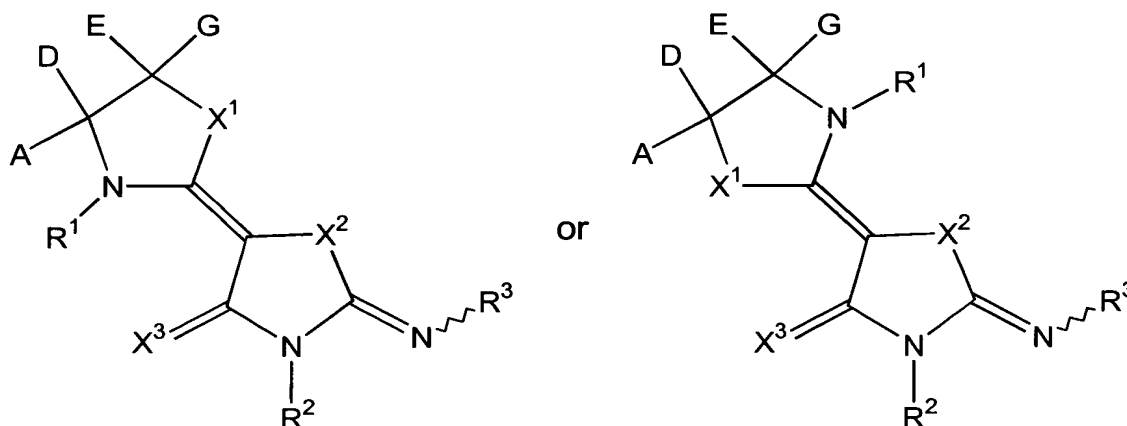


- (b) subsequently, simultaneously, or previously administering one or more of the following: an antihyperlipidemic agent, a plasma HDL-raising agent, an antihypercholesterolemic agent, an HMG-CoA synthase inhibitor, a squalene epoxidase inhibitor, a squalene synthetase inhibitor, an acyl-coenzyme A cholesterol acyltransferase inhibitor, probucol, nicotinic acid or a salt thereof, niacinamide, a cholesterol absorption inhibitor, a bile acid sequestrant anion exchange resin, a low density lipoprotein receptor inducer, a fibrate, vitamin B<sub>6</sub> or a pharmaceutically acceptable salt thereof, vitamin B<sub>12</sub>, vitamin B<sub>3</sub>, an anti-oxidant vitamin, a beta-blocker, an angiotensin II antagonist, an angiotensin converting enzyme inhibitor, a platelet aggregation inhibitor, or aspirin.

45. A method of treating, preventing, or ameliorating obesity or complications thereof, comprising administering a pharmaceutical composition of claim 25.

- 15 46. A method of treating, preventing, or ameliorating obesity or complications thereof, comprising:

(a) administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

- 20 A, D, E and G are selected from (i) or (ii) as follows:
- (i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or
- 25

unsubstituted heteroaryl, substituted or unsubstituted aralkyl,  
 substituted or unsubstituted heteroaralkyl, substituted or unsubstituted  
 heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo,  
 pseudohalo,  $\text{OR}^{10}$ ,  $\text{SR}^{10}$ ,  $\text{S(=O)R}^{13}$ ,  $\text{S(=O)}_2\text{R}^{13}$ ,  $\text{NR}^{11}\text{R}^{12}$  and  $\text{C(=J)R}^{13}$ ,  
 5 or A and G together form substituted or unsubstituted alkylene,  
 substituted or unsubstituted azaalkylene, substituted or unsubstituted  
 oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or  
 unsubstituted alkenylene, substituted or unsubstituted alkynylene,  
 substituted or unsubstituted 1,3-butadienylene, substituted or  
 10 unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted  
 2-aza-1,3-butadienylene;

D and E are each independently selected from hydrogen,  
 substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,  
 substituted or unsubstituted alkynyl, substituted or unsubstituted  
 15 cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or  
 unsubstituted cycloalkylalkyl, substituted or unsubstituted  
 heterocyclylalkyl, substituted or unsubstituted aryl, substituted or  
 unsubstituted heteroaryl, substituted or unsubstituted aralkyl,  
 substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D  
 20 and E together form a bond; or

(ii) A and D; or E and G; together form substituted or unsubstituted  
 alkylene, substituted or unsubstituted azaalkylene, substituted or  
 unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene;  
 and the others of A, D, E and G are selected as in (i);

25  $\text{X}^1$  and  $\text{X}^2$  are each independently selected from O, S,  $\text{S(=O)}$ ,  $\text{S(=O)}_2$ ,  
 Se,  $\text{NR}^5$ ,  $\text{CR}^6\text{R}^7$  and  $\text{CR}^8=\text{CR}^9$ ;

$\text{X}^3$  is O, S, Se,  $\text{NR}^5$  or  $\text{CR}^6\text{R}^7$ ;

$\text{R}^1$  and  $\text{R}^2$  are each independently selected from hydrogen, substituted  
 or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or  
 30 unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or  
 unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,  
 substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted  
 aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted

aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;

- $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or
- 5 unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted
- 10 aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;
- where

- $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl,
- 15 substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo,
- 20 pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

- $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,
- 25 substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

J is O, S or  $NR^{14}$ ;

- $R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl,
- 30 substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted

or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo, OR<sup>16</sup> and NR<sup>14</sup>R<sup>15</sup>;

R<sup>14</sup>, R<sup>15</sup> and R<sup>16</sup> are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

- where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclylalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G, R<sup>1</sup>, R<sup>2</sup>, R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, R<sup>9</sup>, R<sup>10</sup>, R<sup>11</sup>, R<sup>12</sup> and R<sup>13</sup> are unsubstituted or substituted with one or more substituents each independently selected from Q<sup>1</sup>, where Q<sup>1</sup> is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxy carbonyl, alkoxy carbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxy carbonyl, aralkoxy carbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl,

- arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino,
- 5** arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,
- 10** hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyno, isothiocyno, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminoalkylsulfonyloxy,
- 15** alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminoalkylsulfonyl or alkylarylaminosulfonyl; or two  $Q^1$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or
- 20** alkylenedithioxy where y is 1 or 2; or two  $Q^1$  groups, which substitute the same atom, together form alkylene; and
- each  $Q^1$  is independently unsubstituted or substituted with one or more substituents each independently selected from  $Q^2$ ;
- each  $Q^2$  is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile,
- 25** nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkylidiarylsilyl,
- 30** triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl,

- arylaminocarbonyl, diarylamino carbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy,
- 5** aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylamino carbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-
- 10** diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocabonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,
- 15** alkylarylaminooalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxy arylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,
- 20** heterocyclylsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,
- 25** hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylamino sulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl,
- 30** diarylamino sulfonyl or alkylarylaminosulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;

each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;

$R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl,

- 5 aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;

$R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclalkyl;

- 10  $R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclalkyl; and

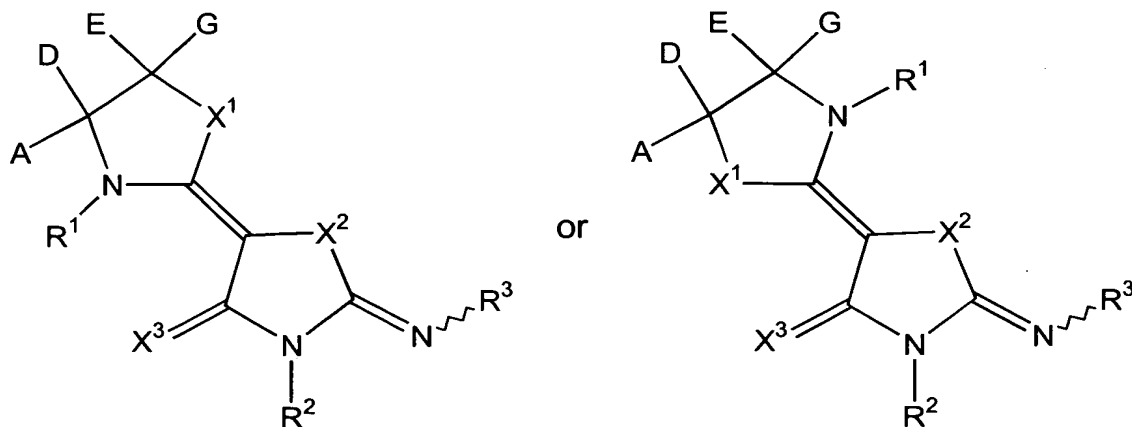
$R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ ; and

- (b) subsequently, simultaneously, or previously administering one or more of the following: phenylpropanolamine, phentermine, diethylpropion, 15 mazindol, fenfluramine, dexfenfluramine, phentiramine, a  $\beta_3$  adrenoceptor agonist, sibutramine, a gastrointestinal lipase inhibitor, a leptin, neuropeptide Y, enterostatin, cholecystokinin, bombesin, amylin, a histamine  $H_3$  receptor, a dopamine  $D_2$  receptor, melanocyte stimulating hormone, corticotrophin releasing factor, galanin or gamma amino butyric acid.

- 20 47. A method of treating, preventing, or ameliorating one or more symptoms of cholestasis, comprising administering a pharmaceutical composition of claim 27.

48. A method of treating, preventing, or ameliorating one or more symptoms of cholestasis, comprising:

- 25 (a) administering a compound of formulae I:



or a pharmaceutically acceptable derivative thereof, wherein:

A, D, E and G are selected from (i) or (ii) as follows:

- (i) A and G are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ , or A and G together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, substituted or unsubstituted thiaalkylene, substituted or unsubstituted alkenylene, substituted or unsubstituted alkynylene, substituted or unsubstituted 1,3-butadienylene, substituted or unsubstituted 1-aza-1,3-butadienylene, or substituted or unsubstituted 2-aza-1,3-butadienylene;
- D and E are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond; or
- (ii) A and D; or E and G; together form substituted or unsubstituted alkylene, substituted or unsubstituted azaalkylene, substituted or unsubstituted oxaalkylene, or substituted or unsubstituted thiaalkylene; and the others of A, D, E and G are selected as in (i);



$X^1$  and  $X^2$  are each independently selected from O, S, S(=O), S(=O)<sub>2</sub>, Se, NR<sup>5</sup>, CR<sup>6</sup>R<sup>7</sup> and CR<sup>8</sup>=CR<sup>9</sup>;

$X^3$  is O, S, Se, NR<sup>5</sup> or CR<sup>6</sup>R<sup>7</sup>;

- $R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;

- $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl, OR<sup>10</sup>, SR<sup>10</sup>, S(=O)R<sup>13</sup>, S(=O)<sub>2</sub>R<sup>13</sup>, NR<sup>11</sup>R<sup>12</sup> and C(=J)R<sup>13</sup>;
- where

- $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo, OR<sup>10</sup>, NR<sup>14</sup>R<sup>15</sup> and C(=J)R<sup>13</sup>;

- $R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,

substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;

J is O, S or  $NR^{14}$ ;

- 5**  $R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocycl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;

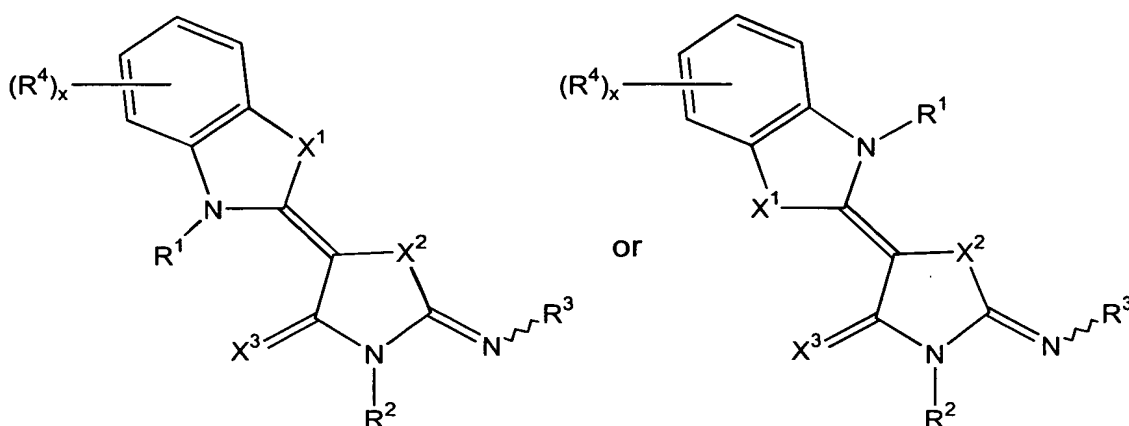
$R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;

- 15** where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocycl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of A, D, E, G,  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or more substituents each independently selected from  $Q^1$ , where  $Q^1$  is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocycl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy,
- 20**
- 25**
- 30**

- aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, imino, hydroxyimino, alkoxyimino, aryloxyimino, aralkoxyimino, alkylazo, arylazo, aralkylazo, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio,
- hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfonyloxy, alkylsulfonyloxy, arylsulfonyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^1$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^1$  groups, which substitute the same atom, together form alkylene; and
- each  $Q^1$  is independently unsubstituted or substituted with one or more substituents each independently selected from  $Q^2$ ;

- each Q<sup>2</sup> is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl,
- 5** cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl,
- 10** arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy,
- 15** aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-
- 20** diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocabonyl, alkylaminothiocabonyl, arylaminothiocabonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,
- 25** alkylarylaminalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,
- 30** heterocyclylsulfonylamino, heteroarylthio, azido, -N<sup>+</sup>R<sup>51</sup>R<sup>52</sup>R<sup>53</sup>, P(R<sup>50</sup>)<sub>2</sub>, P(=O)(R<sup>50</sup>)<sub>2</sub>, OP(=O)(R<sup>50</sup>)<sub>2</sub>, -NR<sup>60</sup>C(=O)R<sup>63</sup>, dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano,

- alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^2$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or alkylenedithioxy where y is 1 or 2; or two  $Q^2$  groups, which substitute the same atom, together form alkylene;
- each  $Q^2$  is independently unsubstituted or substituted with one or more substituents each independently selected from alkyl, halo and pseudohalo;
- $R^{50}$  is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ , where  $R^{70}$  and  $R^{71}$  are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or  $R^{70}$  and  $R^{71}$  together form alkylene, azaalkylene, oxaalkylene or thiaalkylene;
- $R^{51}$ ,  $R^{52}$  and  $R^{53}$  are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;
- $R^{60}$  is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and
- $R^{63}$  is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or  $-NR^{70}R^{71}$ ; and
- (b) subsequently, simultaneously, or previously administering one or more of the following: ursodeoxycholic acid, a corticosteroid, an anti-infective agent, an anti-viral agent, vitamin D, vitamin A, phenobarbital, cholestyramine, UV light, an antihistamine, an oral opiate receptor antagonist or a biphosphate.
49. A method of treating, preventing, or ameliorating the symptoms of a disease or disorder that is modulated or otherwise affected by nuclear receptor activity or in which nuclear receptor activity is implicated, comprising administering a compound of formulae III:



or a pharmaceutically acceptable derivative thereof, wherein:

- each  $R^4$  is independently substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted guanidino, substituted or unsubstituted isothioureido, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  or  $C(=J)R^{13}$ ;

$x$  is an integer from 0 to 4; and

- the amino, alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of  $R^4$  are unsubstituted or substituted with one or more substituents each independently selected from  $Q^2$ .

50. The method of claim 49, wherein  $X^2$  is S and  $X^3$  is O.
51. The method of claim 50, wherein  $X^1$  is S.
52. The method of claim 51, wherein  $R^1$  is substituted or unsubstituted alkyl.
53. The method of claim 52, wherein  $R^2$  is substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl.
54. The method of claim 53, wherein  $R^3$  is substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.

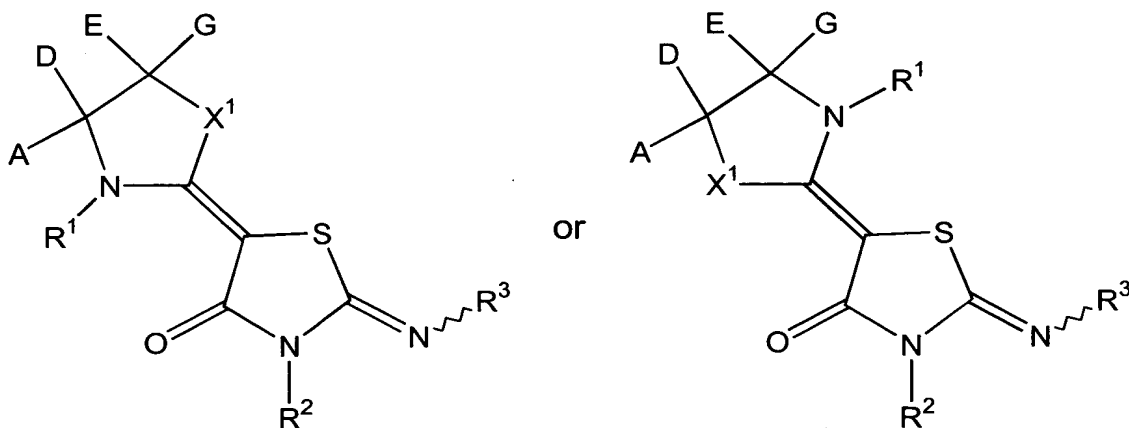
55. The method of claim 50, wherein  $X^1$  is  $CR^8=CR^9$ .

56. The method of claim 55, wherein  $R^1$  is substituted or unsubstituted alkyl.

57. The method of claim 56, wherein  $R^2$  is substituted or  
 5 unsubstituted alkyl, or substituted or unsubstituted aralkyl.

58. The method of claim 57, wherein  $R^3$  is substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.

59. A method of treating, preventing, or ameliorating the symptoms of a disease or disorder that is modulated or otherwise affected by nuclear  
 10 receptor activity or in which nuclear receptor activity is implicated, comprising administering a compound of formulae II:



or a pharmaceutically acceptable derivative thereof, wherein:

A and G are each independently selected from hydrogen, substituted  
 15 or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclylalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted  
 20 aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl, halo, pseudohalo,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;

D and E are each independently selected from hydrogen, substituted or  
 25 unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl,

substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo and pseudohalo or D and E together form a bond;

5  $X^1$  is S;

$R^1$  and  $R^2$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted cycloalkylalkyl,

10 substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroarylium, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;

15  $R^3$  is hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted heteroarylium, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, substituted or unsubstituted heteroaryliumalkyl,  $OR^{10}$ ,  $SR^{10}$ ,  $S(=O)R^{13}$ ,  $S(=O)_2R^{13}$ ,  $NR^{11}R^{12}$  and  $C(=J)R^{13}$ ;

20 where:

$R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$  and  $R^9$  are each independently selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, halo, pseudohalo,  $OR^{10}$ ,  $NR^{14}R^{15}$  and  $C(=J)R^{13}$ ;

25

30

$R^{10}$ ,  $R^{11}$  and  $R^{12}$  are each independently hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or



- unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted
- 5 aralkyl, substituted or unsubstituted heteroaralkyl or  $C(=J)R^{13}$ ;  
 J is O, S or  $NR^{14}$ ;  
 $R^{13}$  is selected from hydrogen, substituted or unsubstituted alkyl, substituted or unsubstituted alkenyl, substituted or unsubstituted alkynyl, substituted or unsubstituted cycloalkyl, substituted or unsubstituted
- 10 heterocyclyl, substituted or unsubstituted cycloalkylalkyl, substituted or unsubstituted heterocyclalkyl, substituted or unsubstituted aryl, substituted or unsubstituted heteroaryl, substituted or unsubstituted aralkyl, substituted or unsubstituted heteroaralkyl, pseudohalo,  $OR^{16}$  and  $NR^{14}R^{15}$ ;  
 $R^{14}$ ,  $R^{15}$  and  $R^{16}$  are each independently selected from hydrogen, alkyl,
- 15 alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, aralkyl and heteroaralkyl;  
 where the alkyl, alkenyl, alkynyl, cycloalkyl, heterocyclyl, cycloalkylalkyl, heterocyclalkyl, aryl, heteroaryl, heteroarylium, aralkyl, heteroaralkyl and heteroaryliumalkyl moieties of  $R^1$ ,  $R^2$ ,  $R^3$ ,  $R^5$ ,  $R^6$ ,  $R^7$ ,  $R^8$ ,  $R^9$ ,
- 20  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$  and  $R^{13}$  are unsubstituted or substituted with one or more substituents each independently selected from  $Q^1$ , where  $Q^1$  is halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl
- 25 containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl,
- 30 aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclxyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy,

- aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxy carbonyloxy, aryloxy carbonyloxy, aralkoxy carbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido,
- 5** ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino,
- 10** arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxy carbonylamino, aralkoxy carbonylamino, arylcarbonylamino,
- 15** arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxy arylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl,
- 20** hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxy sulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy,
- 25** alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxy sulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two  $Q^1$  groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy, thioalkylenoxy or
- 30** alkylenedithioxy; or two  $Q^1$  groups, which substitute the same atom, together form alkylene;

each  $Q^1$  is independently unsubstituted or substituted with one or more substituents each independently selected from  $Q^2$ ;

- each  $Q^2$  is independently halo, pseudohalo, hydroxy, oxo, thia, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl,
- 5** cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl,
- 10** arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy,
- 15** aralkoxycarbonyloxy, aminocarbonyloxy, alkylaminocarbonyloxy, dialkylaminocarbonyloxy, alkylarylaminocarbonyloxy, diarylaminocarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-
- 20** diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocabonyl, alkylaminothiocabonyl, arylaminothiocabonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,
- 25** alkylarylaminalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,
- 30** heterocyclylsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano,

alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, 5 arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl; or two Q<sup>2</sup> groups, which substitute atoms in a 1,2 or 1,3 arrangement, together form alkylenedioxy (*i.e.*, -O-(CH<sub>2</sub>)<sub>y</sub>-O-), thioalkylenoxy (*i.e.*, -S-(CH<sub>2</sub>)<sub>y</sub>-O-) or alkylenedithioxy (*i.e.*, 10 -S-(CH<sub>2</sub>)<sub>y</sub>-S-) where y is 1 or 2; or two Q<sup>2</sup> groups, which substitute the same atom, together form alkylene;

R<sup>50</sup> is hydroxy, alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>, where R<sup>70</sup> and R<sup>71</sup> are each independently hydrogen, alkyl, aralkyl, aryl, heteroaryl, heteroaralkyl or heterocyclyl, or R<sup>70</sup> and R<sup>71</sup> together form 15 alkylene, azaalkylene, oxaalkylene or thiaalkylene;

R<sup>51</sup>, R<sup>52</sup> and R<sup>53</sup> are each independently hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl;

R<sup>60</sup> is hydrogen, alkyl, aryl, aralkyl, heteroaryl, heteroaralkyl, heterocyclyl or heterocyclylalkyl; and

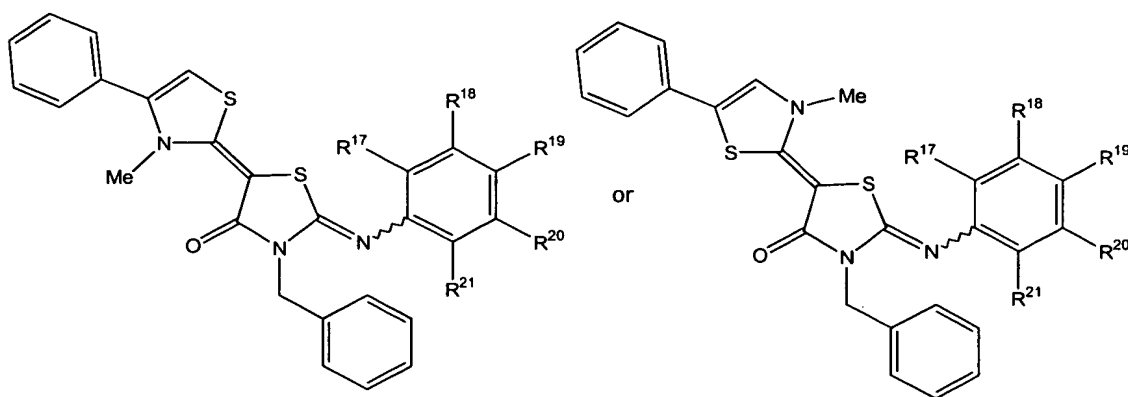
20 R<sup>63</sup> is alkoxy, aralkoxy, alkyl, heteroaryl, heterocyclyl, aryl or -NR<sup>70</sup>R<sup>71</sup>.

60. The method of claim 59, wherein R<sup>1</sup> is substituted or unsubstituted alkyl.

61. The method of claim 60, wherein R<sup>2</sup> is substituted or unsubstituted alkyl, or substituted or unsubstituted aralkyl.

25 62. The method of claim 61, wherein R<sup>3</sup> is substituted or unsubstituted aryl, or substituted or unsubstituted heteroaryl.

63. The method of claim 59, wherein the compound has formulae VI:

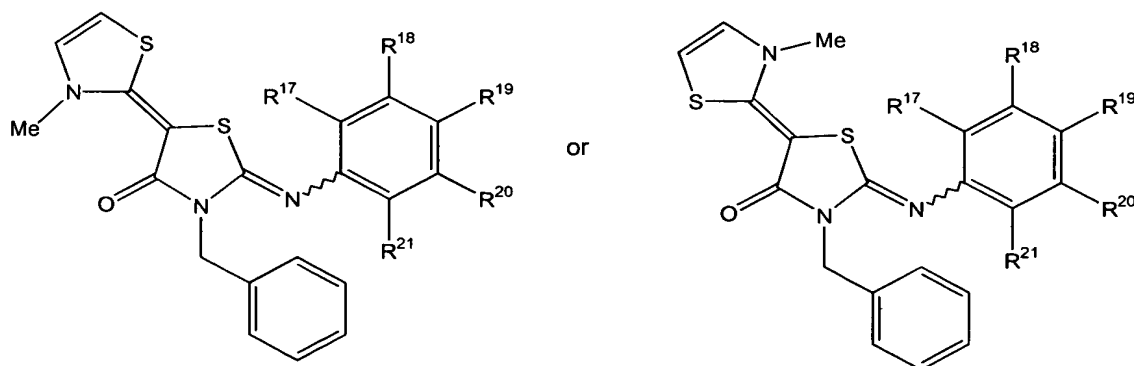


or a pharmaceutically acceptable derivative thereof, where  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  are each independently selected from hydrogen, halo, pseudohalo, hydroxyl, nitrile, nitro, formyl, mercapto, hydroxycarbonyl,

- 5 hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl,
- 10 arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy,
- 15 heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido,
- 20 amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl,
- 25 alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino,

- diarylamino, alkylaryl amino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino,
- 5 heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy,
- 10 hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl,
- 15 diarylaminosulfonyl or alkylarylaminosulfonyl, or any two of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$ , which substitute adjacent carbons on the ring, together form alkylenedioxy; and
- the aryl and heteroaryl groups of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  are unsubstituted or substituted with one or more substituents each independently
- 20 selected from  $R^{30}$ , where  $R^{30}$  is alkyl, halo, pseudohalo, alkoxy, aryloxy or alkylenedioxy.

64. The method of claim 59, wherein the compound has formulae VII:



- 25 or a pharmaceutically acceptable derivative thereof, where  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  are each independently selected from hydrogen, halo, pseudohalo, hydroxyl, nitrile, nitro, formyl, mercapto, hydroxycarbonyl,

- hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl,
- 5** alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl,
- 10** arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-
- 15** dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocabonyl,
- 20** alkylaminothiocabonyl, arylaminothiocabonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl,
- 25** aryloxy carbonylaminoalkyl, aryloxy arylcarbonylamino, aryloxy carbonylamino, alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclylsulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio,
- 30** perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano, alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy,

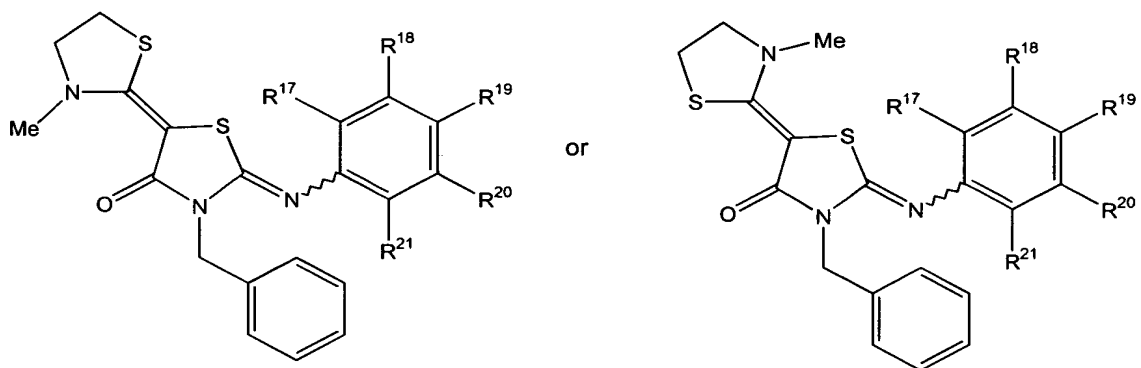
diarylaminosulfonyloxy, alkylarylamino sulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl, alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylamino sulfonyl or alkylarylamino sulfonyl, or any two of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$

- 5 and  $R^{21}$ , which substitute adjacent carbons on the ring, together form alkylenedioxy; and

the aryl and heteroaryl groups of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  are unsubstituted or substituted with one or more substituents each independently selected from  $R^{30}$ , where  $R^{30}$  is alkyl, halo, pseudohalo, alkoxy, aryloxy or

- 10 alkylenedioxy.

65. The method of claim 59, wherein the compound has formulae VIII:



or a pharmaceutically acceptable derivative thereof, where  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$

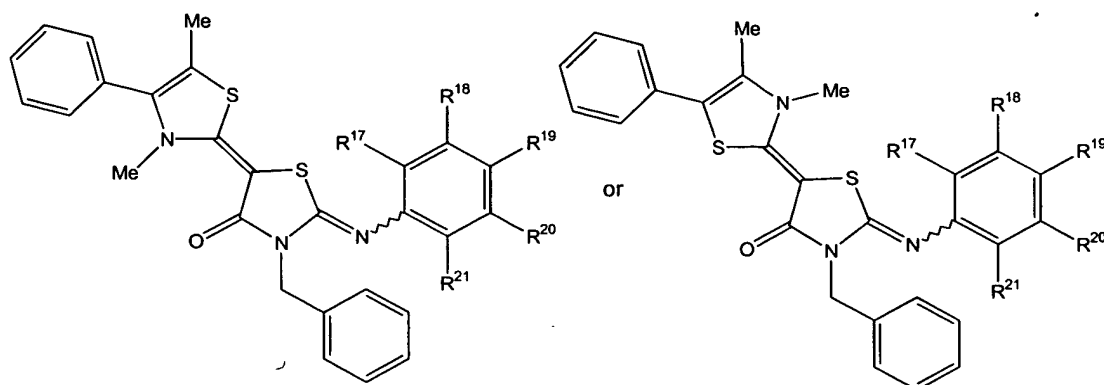
- 15 and  $R^{21}$  are each independently selected from hydrogen, halo, pseudohalo, hydroxyl, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclalkyl, aryl, heteroaryl,
- 20 aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyldiarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxy carbonyl, aryloxy carbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl,
- 25 dialkylaminocarbonyl, arylaminocarbonyl, diarylamino carbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocyclyloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy,



- aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxy carbonyloxy, aralkoxycarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl,
- 10** alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl, alkylarylaminominoalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylaminomino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxy carbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxy carbonylamino,
- 15** alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano,
- 20** alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylamino sulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl,
- 25** alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylamino sulfonyl or alkylarylaminosulfonyl, or any two of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$ , which substitute adjacent carbons on the ring, together form alkylenedioxy; and
- the aryl and heteroaryl groups of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  are
- 30** unsubstituted or substituted with one or more substituents each independently selected from  $R^{30}$ , where  $R^{30}$  is alkyl, halo, pseudohalo, alkoxy, aryloxy or alkylenedioxy.

66. The method of claim 59, wherein the compound has formulae

IX:



- or a pharmaceutically acceptable derivative thereof, where R<sup>17</sup>, R<sup>18</sup>, R<sup>19</sup>, R<sup>20</sup> and R<sup>21</sup> are each independently selected from hydrogen, halo, pseudohalo, hydroxyl, nitrile, nitro, formyl, mercapto, hydroxycarbonyl, hydroxycarbonylalkyl, alkyl, haloalkyl, polyhaloalkyl, aminoalkyl, diaminoalkyl, alkenyl containing 1 to 2 double bonds, alkynyl containing 1 to 2 triple bonds, cycloalkyl, cycloalkylalkyl, heterocyclyl, heterocyclylalkyl, aryl, heteroaryl, aralkyl, aralkenyl, aralkynyl, heteroarylalkyl, trialkylsilyl, dialkylarylsilyl, alkyl diarylsilyl, triarylsilyl, alkylidene, arylalkylidene, alkylcarbonyl, arylcarbonyl, heteroarylcarbonyl, alkoxycarbonyl, alkoxycarbonylalkyl, aryloxycarbonyl, aryloxycarbonylalkyl, aralkoxycarbonyl, aralkoxycarbonylalkyl, arylcarbonylalkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, arylaminocarbonyl, diarylaminocarbonyl, arylalkylaminocarbonyl, alkoxy, aryloxy, heteroaryloxy, heteroaralkoxy, heterocycloxy, cycloalkoxy, perfluoroalkoxy, alkenyloxy, alkynyloxy, aralkoxy, alkylcarbonyloxy, arylcarbonyloxy, aralkylcarbonyloxy, alkoxycarbonyloxy, aryloxycarbonyloxy, aralkoxycarbonyloxy, guanidino, isothioureido, ureido, N-alkylureido, N-arylureido, N'-alkylureido, N',N'-dialkylureido, N'-alkyl-N'-arylureido, N',N'-diarylureido, N'-arylureido, N,N'-dialkylureido, N-alkyl-N'-arylureido, N-aryl-N'-alkylureido, N,N'-diarylureido, N,N',N'-trialkylureido, N,N'-dialkyl-N'-arylureido, N-alkyl-N',N'-diarylureido, N-aryl-N',N'-dialkylureido, N,N'-diaryl-N'-alkylureido, N,N',N'-triarylureido, amidino, alkylamidino, arylamidino, aminothiocarbonyl, alkylaminothiocarbonyl, arylaminothiocarbonyl, amino, aminoalkyl, alkylaminoalkyl, dialkylaminoalkyl, arylaminoalkyl, diarylaminoalkyl,

- alkylarylaminooalkyl, alkylamino, dialkylamino, haloalkylamino, arylamino, diarylamino, alkylarylamino, alkylcarbonylamino, alkoxycarbonylamino, aralkoxycarbonylamino, arylcarbonylamino, arylcarbonylaminoalkyl, aryloxycarbonylaminoalkyl, aryloxyarylcarbonylamino, aryloxycarbonylamino,
- 5** alkylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heterocyclisulfonylamino, heteroarylthio, azido,  $-N^+R^{51}R^{52}R^{53}$ ,  $P(R^{50})_2$ ,  $P(=O)(R^{50})_2$ ,  $OP(=O)(R^{50})_2$ ,  $-NR^{60}C(=O)R^{63}$ , dialkylphosphonyl, alkylarylphosphonyl, diarylphosphonyl, hydroxyphosphonyl, alkylthio, arylthio, perfluoroalkylthio, hydroxycarbonylalkylthio, thiocyano, isothiocyano,
- 10** alkylsulfinyloxy, alkylsulfonyloxy, arylsulfinyloxy, arylsulfonyloxy, hydroxysulfonyloxy, alkoxysulfonyloxy, aminosulfonyloxy, alkylaminosulfonyloxy, dialkylaminosulfonyloxy, arylaminosulfonyloxy, diarylaminosulfonyloxy, alkylarylaminosulfonyloxy, alkylsulfinyl, alkylsulfonyl, arylsulfinyl, arylsulfonyl, hydroxysulfonyl, alkoxysulfonyl, aminosulfonyl,
- 15** alkylaminosulfonyl, dialkylaminosulfonyl, arylaminosulfonyl, diarylaminosulfonyl or alkylarylaminosulfonyl, or any two of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$ , which substitute adjacent carbons on the ring, together form alkylenedioxy; and
- the aryl and heteroaryl groups of  $R^{17}$ ,  $R^{18}$ ,  $R^{19}$ ,  $R^{20}$  and  $R^{21}$  are
- 20** unsubstituted or substituted with one or more substituents each independently selected from  $R^{30}$ , where  $R^{30}$  is alkyl, halo, pseudohalo, alkoxy, aryloxy or alkylenedioxy.